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CONCISE DEFINITIVE REVIEW

Bram Rochwerg, MD, MSc (Epi), FRCPC, Series Editor

Assessment of Tissue Perfusion Pressure in Patients With Septic Shock: Beyond Mean Arterial Pressure

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OBJECTIVES: Optimization of macrohemodynamics is just the starting point in the management of hemodynamics in patients with septic shock. We describe the interaction between the various determinants of arterial pressure and tissue perfusion, how to optimize them and their estimations at the bedside. This is a concise definitive review of the assessment of tissue perfusion pressure (TPP) in patients with septic shock beyond just mean arterial pressure (MAP).

DATA SOURCES: Original publications were retrieved through a PubMed and MEDLINE databases with search terms related to septic shock, arterial blood pressure, critical closing pressure (Pcc), mean systemic filling pressure (Pmsf), and TPP. Supporting evidence was also retrieved from PubMed and MEDLINE when indicated.

STUDY SELECTION: English-language systematic reviews, narrative reviews, meta-analyses, randomized clinical trials, and observational studies.

DATA EXTRACTION AND DATA SYNTHESIS: Data from relevant publications were reviewed, selected, and summarized by the authors and applied as indicated.

CONCLUSIONS: The relationship between arterial pressure and outcomes in septic shock is complex and heterogeneous. Focusing on critical parameters—such as TPP, the vascular waterfall, and individual treatment effects—enables a more personalized approach, focused on perfusion rather than pressure alone. Persistent hypoperfusion despite adequate macrocirculatory targets marks a pivotal moment when microcirculatory assessment becomes essential to guide therapy and avoid potentially harmful escalation of fluids or vasopressors. Bedside measurements of systolic arterial pressure, MAP, diastolic arterial pressure, Pcc, and Pmsf offer practical tools for monitoring and tailoring treatment. Future clinical trials are needed to validate these metrics and refine resuscitation strategies in septic shock.

KEYWORDS: arterial blood pressure; critical closing pressure; mean systemic filling pressure; septic shock; tissue perfusion pressure

Septic shock is a life-threatening condition (1) associated with vasoplegia that impairs tissue perfusion, leading to organ dysfunction and death (2). Both the depth and duration of arterial hypotension impact mortality (3–5). Restoring mean arterial pressure (MAP) and cardiac output (CO) to threshold targets by fluids and vasopressors may not restore organ function or tissue perfusion (6–8). The dissociation between measurable macrocirculatory parameters and microcirculatory flow warrants deeper analysis of arterial pressure and tissue blood flow determinants.

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KEY POINTS

Question: Can we assess tissue perfusion pressure (TPP) and vasomotor tone in patients with septic shock beyond mean arterial pressure (MAP)?

Findings: MAP relative to critical closing pressure (Pcc) defines TPP, while the pressure gradient between Pcc and mean systemic filling pressure (Pmsf) defines the vascular waterfall essential to allow for autoregulation of local flow. Low vasomotor tone is characterized by a decrease in diastolic arterial pressure. Importantly, tachycardia, by limiting diastolic runoff time, minimizes hypotension, which is good, but masks vasoplegia. To the extent that hemodynamic factors in sepsis create inadequate tissue perfusion, resuscitation efforts that restore both TPP and local vascular waterfalls should improve the linkage between macrocirculatory parameters, such as MAP and cardiac output, with microcirculatory measures of tissue perfusion. This broader view of the determinants of septic shock-induced tissue hypoperfusion should allow for a more nuanced approach to the use of fluids, vasopressors, and inotropes.

Meaning: Arterial blood pressure measures and their derived tissue perfusion parameters may be estimated at the bedside and could potentially guide clinical decision-making beyond MAP in patients with septic shock.

ARTERIAL PRESSURE AND THE DETERMINANTS OF ORGAN BLOOD FLOW

Arterial pressure is not a single number nor solely defines pathology or organ perfusion. Understanding its determinants is crucial for clinical decision-making. The four main parameters defining the arterial profile are systolic arterial pressure (SAP), diastolic arterial pressure (DAP), pulse pressure (PP), and MAP (9) (**Fig. 1**). SAP is the peak pressure from left ventricular (LV) ejection, arterial tone, reflected waves, and arterial viscoelastic properties. DAP is the minimal pressure before ejection, determined by central blood volume, vasomotor tone, and heart rate (HR). PP is the difference between DAP and SAP, influenced by stroke volume (SV), compliance, and SAP/DAP

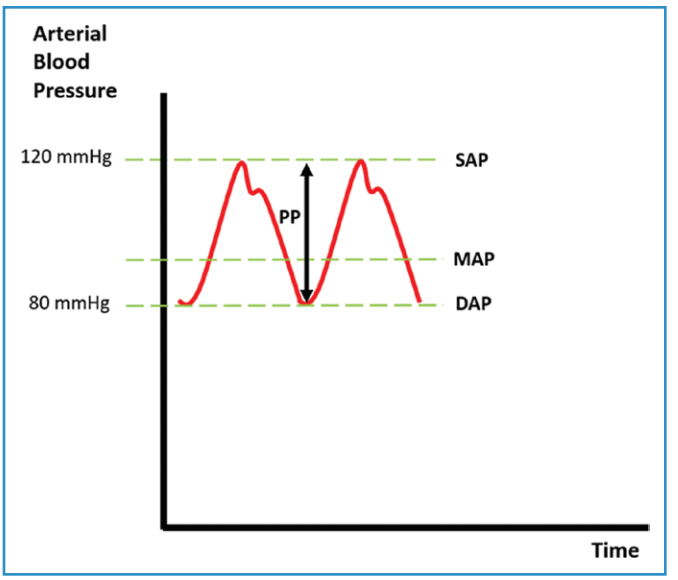

Figure 1. Components of arterial blood pressure. DAP = diastolic arterial pressure, MAP = mean arterial pressure, PP = pulse pressure (systolic arterial pressure–diastolic arterial pressure), SAP = systolic arterial pressure.

factors. MAP, is an arithmetic value of arterial pressure across a heartbeat, is calculated as DAP plus one-third of PP (10).

Consensus definitions of septic shock include hypotension (e.g., SAP ≤ 100 mm Hg) or vasopressor need to maintain MAP (1). Guidelines recommend targeting an initial MAP greater than or equal to 65 mm Hg (11), a reasonable target as SAP varies across the arterial circuit (12–14). SAP site-specific differences may impair resuscitation if minimal SAP is the target. Low DAP reflects vasoplegia; MAP, unlike SAP, is relatively constant throughout the arterial tree and reflects average arterial pressure (10).

MAP constancy down to small arteries/arterioles reflects large vessels' role as capacitors maintaining pressure during diastole with little forward flow. As arteries branch into smaller vessels, the total cross-sectional area increases, vascular resistance rises, and blood pressure drops rapidly over a short distance (15). When intraluminal pressure falls below the vessel wall tone from smooth muscle, vessels collapse. This pressure defines the arterial critical closing pressure (Pcc) (16, 17). The collapse point moves distally with vasomotor tone loss, as in sepsis, or more proximally with tone increase, as in early hemorrhagic or cardiogenic shock (16). Tissues regulate local blood flow by altering vasomotor tone in small feeding arteries/arterioles to meet metabolic demands (18).

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Tissue perfusion pressure (TPP) is the gradient between MAP and Pcc. Blood flow changes occur via feedback-driven tone changes through endothelial retrograde signaling (16). For Pcc changes to affect blood flow, two conditions must be met: TPP must sustain forward flow (19) and Pcc must exceed downstream capillary pressure enough to drive flow (15, 20, 21). Capillaries' large cross-sectional area and slow flow mean minimal back pressure, except for venular pressure. Although Pcc varies by tissue, venular backpressure is relatively constant due to high capacitance and area of drainage vessels and their slow flow (22). This backpressure is called mean systemic filling pressure (Pmsf)—the pressure after abrupt flow cessation and redistribution, estimating upstream pressure driving venous return and correlating with circulatory fullness (23).

Normally, Pmsf is low (≤ 10 mm Hg), and Pcc is high (~45 mm Hg at rest), decreasing with increased metabolic demand. This creates a "vascular waterfall" between arterial inflow (Pcc) and capillaries (24). Pmsf depends on venular tone, tissue pressure, and blood volume. Bedside methods exist to estimate Pmsf (25), and a smartphone app called iGuyton (26) estimates Pmsf and venous return parameters from demographic data, CO, MAP, and right atrial pressure (Pra). The venous return pressure gradient is Pmsf–Pra (10). **Figure 2** illustrates these concepts and their circulation control points.

The vascular waterfall protects capillaries from high pressure and edema. However, increased metabolic demand reduces Pcc and raises capillary pressure, promoting fluid translocation (27). During exercise, local Pcc drops, causing interstitial edema, "muscle bulking" reflects this. Although each tissue has specific Pcc values, a global Pcc estimate can be derived from systemic pressure changes during respiration or sinus pauses (28). MAP, SAP, DAP, Pcc, and Pmsf can be bedside-estimated with non- or minimally invasive

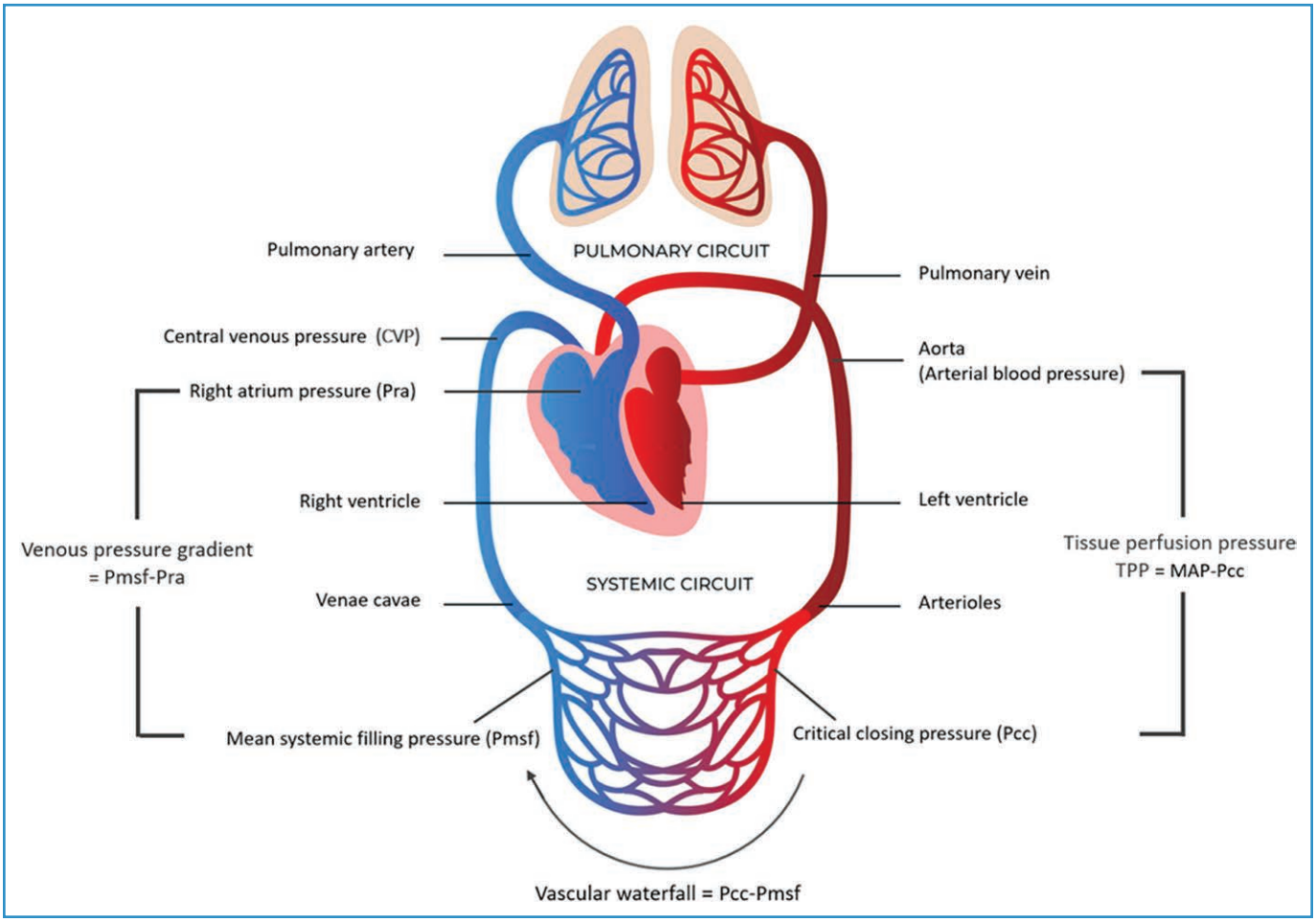

Figure 2. Didactic illustration of different pressures that can be measured at each control point along the circulatory system. CVP = central venous pressure, Pcc = critical closing pressure, Pmsf = mean systemic filling pressure, Pra = right atrial pressure, TPP = tissue perfusion pressure.

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methods, providing a more accurate hemodynamic view for clinicians.

SEPSIS, ARTERIAL PRESSURE, AND AUTOREGULATION

Septic shock induces generalized vasoplegia by blunting vascular endothelial-smooth muscle feedback (2). This decreases both Pcc and Pmsf, but Pcc decreases more due to its unique determinants. Clinically, Pcc may fall to levels near Pmsf (12). In such cases, autoregulation is lost. Although resuscitation may increase MAP and CO, the resulting flow is uniformly distributed, leading to underperfusion of metabolically active tissues and overperfusion of inactive ones. This state is hyperdynamic hypotension: low MAP and DAP, high CO, HR, and mixed venous oxygen saturation, along with hyperlactatemia and organ dysfunction (2).

A DAP less than 40 mm Hg typically indicates vasoplegia since normal Pcc is higher. With prolonged sepsis, systemic inflammation can trigger intracellular metabolic changes that persist despite adequate TPP and vascular waterfall restoration (29, 30). Clinicians may face patients in septic shock with normalized MAP and CO, yet persistent organ dysfunction. Measuring TPP, Pcc, and presence of vascular waterfall may guide further care: either intensifying resuscitation if inadequate or holding support if values are sufficient since more fluids or vasopressors might be harmful. However, this has not been tested in trials.

ADVANCED ARTERIAL PRESSURE METRICS

Ventriculo-Arterial Coupling

The LV ejects SV into a pressurized arterial system. SV generates forward flow, but arterial pressure limits output due to afterload. As impedance increases, SV falls depending on the balance between end-systolic elastance (intrinsic contractility) and arterial elastance (31–33). This relationship—ventriculo-arterial coupling (VAC)—is shown in **Figure 3**. An optimal VAC ratio is close to 1, matching contractility to arterial load, enabling autoregulation with low energy demand (33). Arterial elastance can be estimated as (SAP × 0.9)/SV, assuming a constant HR (31).

Sepsis reduces arterial elastance via vasoplegia (2, 32). Thus, for the same contractility and end-diastolic volume, SV increases while SAP stays constant or decreases. Sepsis may also impair contractility, but this is rarely apparent in early hyperdynamic septic shock, as low arterial elastance masks it. Increasing elastance with vasopressors can reveal poor contractility, seen as reduced CO (31, 33, 34).

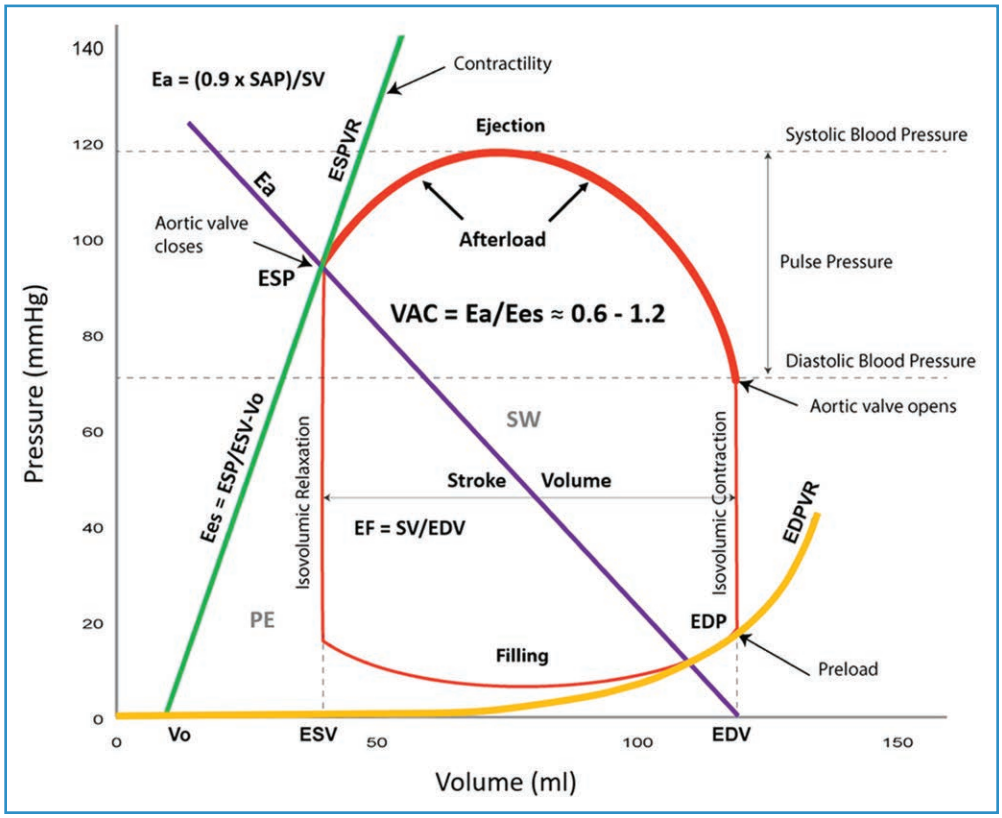

Figure 3. Schematic presentation of ventricular-arterial coupling on the pressure-volume relationship. Ea = arterial elastance, EDP = end-diastolic pressure, EDPVR = end-diastolic pressure-volume relationship, EDV = end-diastolic volume, Ees = end-systolic elastance, EF = ejection fraction, ESP = end-systolic pressure, ESPVR = end-systolic pressure-volume relationship, ESV = end-systolic volume, PE = potential energy, SAP = systolic arterial pressure, SV = stroke volume, SW = stroke work, VAC = ventricular-arterial coupling, Vo = volume axis interception.

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The free smartphone app iElastance (35) estimates end-systolic elastance, arterial elastance, and VAC using SAP, DAP, ejection fraction, SV, pre-ejection time, and ejection time.

Dynamic Arterial Elastance

Changes in LV SV induce proportional changes in PP. This relationship depends on central arterial compliance, termed dynamic arterial elastance (Eadyn) (36). Eadyn is calculated as the ratio of pulse pressure variation (PPV) to SV variation, measured during spontaneous or positive-pressure ventilation (31, 34). Eadyn is related to VAC (37) but primarily assesses how MAP will change with altered CO or vasopressor use (38, 39).

In hypotensive, volume-responsive patients, CO may rise with fluids, but MAP might not increase. This is common in septic shock due to low arterial elastance. If Eadyn is less than 1 before fluid loading, MAP typically increases little. These patients benefit from vasopressors to shorten hypotension duration and reduce fluid needs (34, 40).

Conversely, in vasoplegic patients on vasopressors, it's unclear if support is still needed. Currently, clinicians test weaning by lowering vasopressors and observing MAP. If it falls, the patient is vasopressor-dependent. However, this trial can trigger hypotension and worsen organ injury. If Eadyn is greater than 1.1, vasopressor weaning rarely causes hypotension, enabling safer, faster tapering in stable patients (38, 41–43).

CLINICAL RELEVANCE OF ARTERIAL PRESSURE COMPONENTS

Systolic Arterial Pressure

LV contraction propels blood into the aorta, raising central arterial pressure. This rise occurs during systolic ejection, making SAP a measure of LV performance. Arterial stiffness, or elastance, is a secondary determinant of SAP (15, 44). Additionally, backward-reflected pressure waves from vascular branching points further elevate peripheral SAP (pSAP) (45) (**Fig. 4**). Clinically, SAP is a quick triage marker, easily measured by sphygmomanometry, and commonly used to define hypotension in acute settings.

SAP less than or equal to 100 mm Hg is an early sign of sepsis (1), but it also appears in cardiogenic, hypovolemic, and obstructive shock. Thus, systolic hypotension is a nonspecific marker of circulatory failure (46). Literature on SAP's prognostic value is mixed, but higher SAP often correlates with better outcomes (47). Marked, irregular SAP swings suggest higher mortality risk and are more likely related to fluid deficiency than vasopressor need (48).

Mean Arterial Pressure

MAP is the average arterial pressure during a cardiac cycle, estimated as DAP plus one-third the PP. Normal MAP ranges from 70 to 110 mm Hg (49). In septic shock, 65 mm Hg is considered the minimum initial threshold for end-organ perfusion (50) or no more than 15% below baseline in chronic hypertensive patients (51, 52). Since MAP represents only input pressure, high venous or intra-abdominal pressure may demand a higher MAP to maintain perfusion. It's the TPP, not MAP alone, that determines tissue flow (53, 54).

MAP reflects the overall cycle pressure and is heavily influenced by DAP, as the heart spends more time in diastole.

Diastolic Arterial Pressure

DAP is the lowest arterial pressure during the cardiac cycle. It's influenced by residual arterial volume at diastole's end, vessel tone, and Pcc. Diastolic time impacts this volume, and tachycardia shortens it, raising DAP for the same SV (55–57). Patients with sepsis and chronic hypertension may need a DAP of 54–62 mm Hg for adequate perfusion (52).

Coronary blood flow to the LV occurs during diastole, as systolic contraction compresses coronary vessels. Therefore, DAP is the input pressure for LV perfusion. If DAP falls below 40 mm Hg, myocardial ischemia may occur (58). DAP less than 40 mm Hg is often due to reduced vascular tone, especially in tachycardia (59, 60). Xiao et al (61) identified optimal DAP and HR ranges of 50–70 mm Hg and 60–90 beats/min (bpm) in septic shock. DAP less than or equal to 40 mm Hg with HR greater than or equal to 100 bpm predicts higher mortality.

Holder et al (62) showed DAP less than 52 mm Hg predicts early septic shock progression within 96 hours. Lower DAP indicates greater vasoplegia

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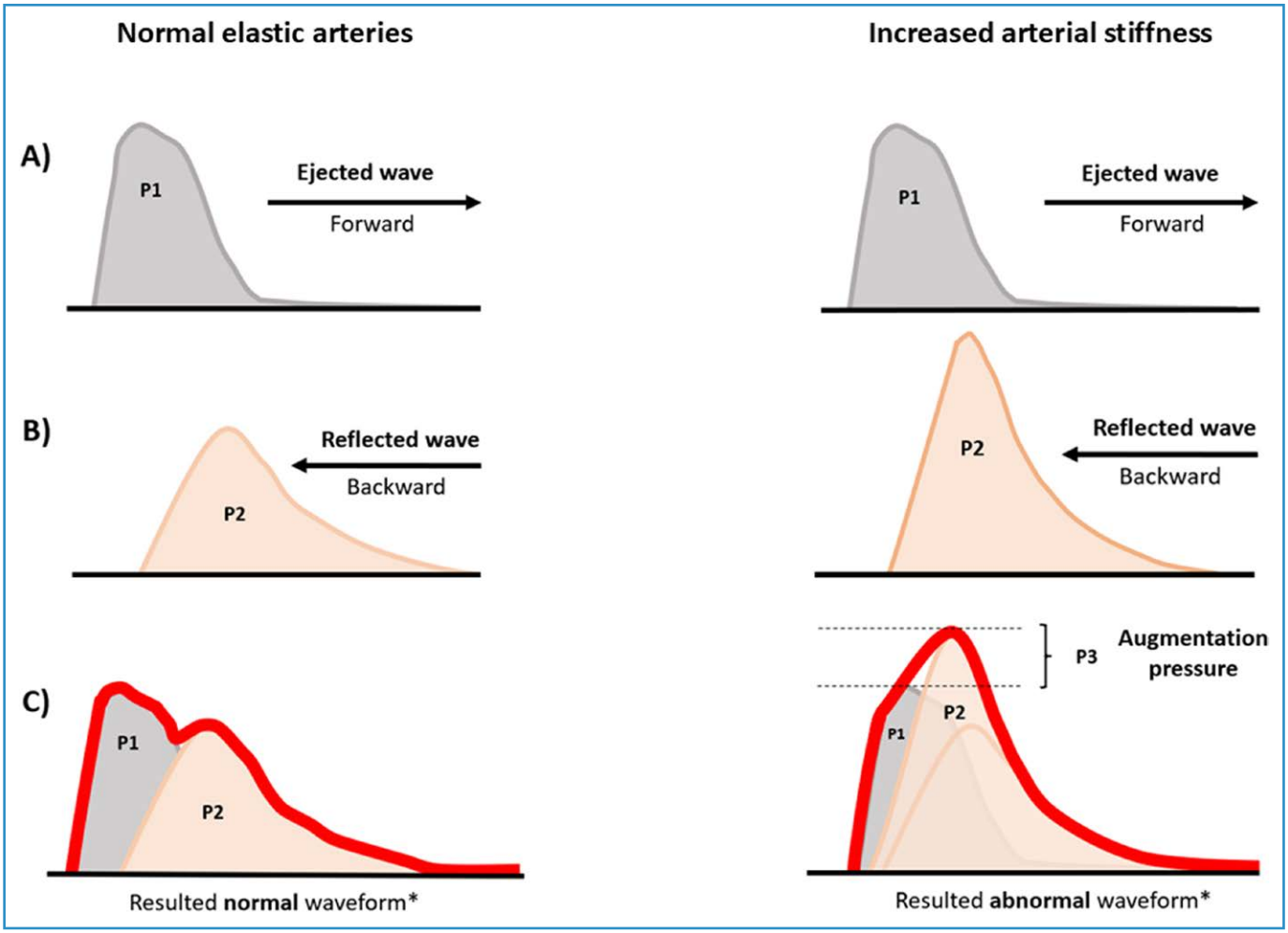

Figure 4. Augmentation pressure phenomenon. **A**, Forward arterial pressure wave. **B**, Reflected pressure wave from arterial reflectance points coming retrograde from the periphery to the central circulation. **C**, Impact of wave reflection on the pressure wave contour increasing systolic blood pressure (augmentation pressure) due to earlier reflected wave in patients with increased arterial stiffness (*right side*). The *red line* shows the resulting arterial waveform. *Resulted normal and abnormal waveforms are directly related to how elastic or stiff (respectively) is the specific artery where blood pressure is being measured. P1 = ejection wave, P2 = reflecting wave, P3 = augmentation pressure.

and worse outcomes. Gao et al (63) found an inverse link between DAP and 28-day mortality post-resuscitation—DAP less than 59 mm Hg at 24 hours correlated with poor survival, suggesting targeting DAP greater than or equal to 59 mm Hg after achieving MAP 65 mm Hg may improve outcomes. This concept is being explored in the ongoing. A multicenter randomized clinical trial designed to compare the effects of peripheral perfusion-targeted resuscitation versus lactate-guided resuscitation on mortality in patients with septic shock (ANDROMEDA-SHOCK-2) trial (64).

Even if MAP exceeds 65 mm Hg, low DAP is still linked to high 90-day mortality (51, 65). Furthermore, microcirculatory dysfunction often persists after MAP normalization (66, 67). Collet et al (68) identified DAP as the only independent determinant of tissue oxygen resaturation in sepsis.

Pulse Pressure

PP is the difference between SAP and DAP. It noninvasively reflects SV relative to vasomotor tone. In sepsis, low PP is tied to higher mortality (69–71). Respiratory-induced changes in PP, or PPV, are common (72). In ventilated patients, PPV greater than or equal to 13% predicts fluid responsiveness with high sensitivity (85–89%) and specificity (88–98%) (73).

Various respiratory maneuvers help evaluate fluid responsiveness using PPV (74). PPV is a simple

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bedside tool to predict and assess the hemodynamic impact of intravascular volume expansion in septic patients.

INFLUENCE OF HEART RATE ON ARTERIAL BLOOD PRESSURE

HR exerts a significant influence on arterial blood pressure (ABP), particularly through its effect on diastolic time. Tachycardia shortens the diastolic phase, thereby limiting arterial runoff and resulting in elevated DAP for the same SV (10). This phenomenon can mask underlying vasoplegia, as the rise in DAP is not due to increased vascular tone but to the reduced time available for diastolic runoff (**Fig. 5**). Reflex tachycardia in critically ill patients may therefore give the false impression of preserved vascular tone.

Wilkinson et al (45) demonstrated that incremental pacing, which increases HR without affecting CO, results in a proportional decrease in SV but still leads to increased SAP, DAP, and MAP. Interestingly, while central DAP increased with pacing, central SAP (cSAP) did not show the same trend, likely due to differences in the timing of reflected pressure waves. This underscores the complex interplay between HR and the components of ABP.

A clinically relevant parameter that integrates HR and DAP is the diastolic shock index (DSI), defined as HR divided by DAP. Ospina-Tascón et al (75) found that a DSI greater than 2.2 was associated with significantly higher mortality in patients with septic shock. The relationship is such that for a constant HR, a lower DAP increases mortality, and for a constant DAP, a higher HR has the same effect. Notably, both HR and DAP are independent predictors of mortality in this setting.

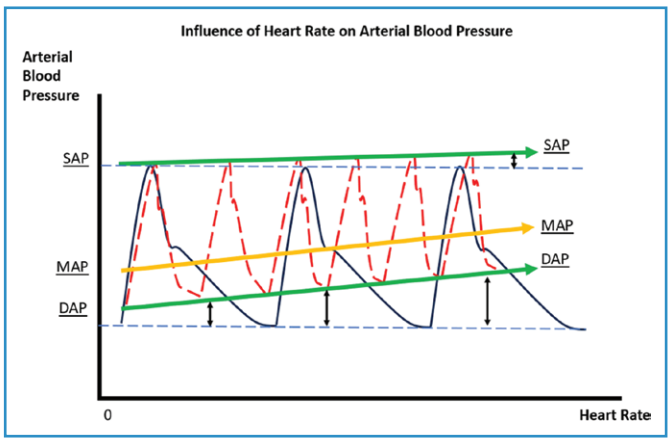

Figure 5. Influence of the heart rate on arterial blood pressure. *Black waves* represent more or less constant values of systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) at normal heart rates. The *red waves* show how as heart rate increases, arterial blood pressure also increases, with a greater increase in DAP than in SAP with respect to the base line values. MAP = mean arterial pressure.

BEDSIDE ARTERIAL PRESSURE MONITORING

Although invasive ABP monitoring is frequently employed in critically ill patients, evidence does not uniformly support its routine use. This is largely because measurements alone, without being used to guide targeted interventions, do not necessarily improve clinical outcomes. Kaufmann et al (76) compared noninvasive and invasive measurements of SAP, MAP, and DAP in patients, including those on norepinephrine infusions, and found no significant differences between the two modalities. However, a meta-analysis by Kim et al (77) concluded that continuous noninvasive ABP monitors tend to be both inaccurate and imprecise beyond acceptable thresholds mainly when the patient is hypotensive (78). These discrepancies are especially relevant when calculating DSI or making critical decisions in hypotensive patients. As a result, invasive arterial monitoring remains the standard recommendation in unstable patients, according to major critical care guidelines.

In vasoconstricted states, peripheral ABP readings may become unreliable. Kim et al (79) showed that in patients receiving greater than or equal to 0.1 μg/kg/min of norepinephrine to maintain MAP greater than or equal to 65 mm Hg, radial artery pressures underestimated femoral artery pressures by greater than or equal to 5 mm Hg in 62.2% of cases. Wisanusattra and Khwannimit (80) reported similar findings. This discrepancy arises because pSAP is often higher than cSAP due to reflected pressure wave amplification (78, 81). Therefore, pSAP is not a reliable surrogate for assessing central hemodynamics or cardiovascular risk (82). To correct for this, Chemla et al (83) proposed an equation to estimate cSAP from peripheral MAP and DAP: $cSAP = MAP^2/DAP$. This approach minimizes reliance on potentially misleading pSAP values. Importantly, noninvasive methods tend to overestimate DAP by

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an average of 6 mm Hg and underestimate SAP by the same amount when compared with invasive measures (84, 85). In vasoplegic states, reflected pressure waves are diminished, causing peripheral measurements to underestimate central pressures even more markedly (86).

TISSUE PERFUSION PRESSURE

TPP, defined as the difference between MAP and the Pcc, reflects the driving force for tissue blood flow. Since Pcc is typically higher than the Pmsf, local vasodilation (which decreases Pcc) can enhance perfusion. This is the primary mechanism by which the body matches local blood flow to metabolic demand through autoregulation.

However, in vasoplegia, Pcc may fall to levels approaching Pmsf, impairing this autoregulatory mechanism. In such cases, even increases in MAP may not improve perfusion. A TPP greater than 34 mm Hg has been associated with better lactate clearance and improved microcirculatory regulation in cardiac surgery patients (19). Andrei et al (87) observed that in postoperative vasoplegic patients, the Pcc–Pmsf gradient was less than 5 mm Hg before resuscitation. Following norepinephrine administration to raise MAP above 80 mm Hg, only half of these patients showed an increase in Pcc, reestablishing a vascular waterfall (Pcc ≫ Pmsf). Those who did showed better perfusion outcomes, including improved lactate clearance, lower delta Pco_2, improved sublingual microcirculatory blood flow, and faster capillary refill time (CRT) (87).

PCC AND PMSF BEDSIDE MEASUREMENT

Multiple bedside techniques have been developed to estimate Pcc and Pmsf (**Table 1**).

Pcc

Each vascular bed has its own Pcc, which varies with metabolic demand. However, a general Pcc can be estimated bedside by rapidly occluding a peripheral arterial catheter (28); the initial arterial pressure decay

TABLE 1.
Bedside Measurement of Critical Closing Pressure and Mean Systemic Filling Pressure

Pcc Bedside Measurement		
Name of Method	**Technique**	**Type of Patient**
Pcc	Peripheral arterial catheter measuring arterial pressure is rapidly occluded. The initial arterial pressure decay during the first 10–12 s (approximates Pcc)	All of them
Pmsf Bedside Measurement		
Name of Method	**Technique**	**Type of Patient**
Pmsf arm	Arm cuff is rapidly inflated stopping forearm flow (arterial and venous) equilibrium pressure corresponds to Pmsf	Awake or sedated Spontaneous breathing or on mechanical ventilation Sinus or cardiac arrhythmias
Pmsf analogue	Guytonian mathematical model using the following formula: Pmcf analogue = a × CVP + b × MAP + c × CO	Awake or sedated Spontaneous breathing or on mechanical ventilation Sinus or cardiac arrhythmias
Pmsf inspiratory hold	End-inspiratory hold maneuvers, simultaneously measure changes in right atrial pressure and cardiac output. The zero right atrial pressure interception value corresponds to Pmsf	Must be on mechanical ventilation with no spontaneous ventilatory efforts Without cardiac arrhythmias

CO = cardiac output, CVP = central venous pressure, MAP = mean arterial pressure, Pcc = critical closing pressure, Pmsf = mean systemic filling pressure.

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over 10–12 seconds approximates Pcc, following a logarithmic decay pattern (88).

Pmsf Arm

Rapid inflation of a cuff (> 50 mm Hg above SAP) around the upper arm transiently equilibrates arterial and venous pressures, reflecting Pmsf (89, 90). A rapid cuff inflator (0.3 s) (91) or pneumatic tourniquet (1.4 s) (92, 93) should be used. Measuring only arterial pressure until it asymptotes (~18–20 s) is often sufficient (91). This method is applicable in awake patients, those on mechanical ventilation, or with arrhythmias.

Pmsf Analogue

Derived mathematically from the Guyton model (CO = VR = [Pmsf–CVP]/RVR) (90, 91, 94–97), where CVP = central venous pressure, RVR = resistance to venous return, and VR = venous return. The Pmsf analogue uses a formula: $Pmsf = a \times CVP + b \times MAP + c \times CO$, where $a + b = 1$, and constants are based on veno-arterial compliance ($a = 0.96$, $b = 0.04$) (94, 96–98). A smartphone app, iGuyton (26), can automate this calculation if CO, MAP, and Pra are known.

Pmsf Inspiratory Hold

This oldest method involves brief end-inspiratory holds (2–10 cm H_2O for 6–10 s), plotting Pra against CO. The zero-flow intercept indicates Pmsf (89, 90). It requires controlled mechanical ventilation without spontaneous breaths or arrhythmias.

ARTERIAL BLOOD PRESSURE AND MACRO-TO-MICROCIRCULATORY COUPLING

Macro-to-microcirculatory coupling (or hemodynamic coherence) refers to the concept where improving systemic macrocirculatory variables, such as MAP and CO, leads to concurrent improvements in microcirculatory flow and reversal of tissue hypoperfusion (99). However, in septic shock, achieving these macrocirculatory targets does not always result in adequate tissue perfusion to meet the metabolic demands of tissues (6). The relationship between increased MAP and microcirculatory perfusion improvement can be variable. The improvement largely depends on factors such as the balance between systemic TPP reaching a minimal threshold and the existence of a vascular waterfall between the Pcc and the Pmsf, where a decrease in Pcc leads to increased blood flow (100).

Assessing microcirculatory flow at the bedside is challenging. Studies have shown that after increasing MAP to 80–85 mm Hg in hypotensive septic shock patients, microvascular flow responses are heterogeneous. Patients with initially low microvascular flow tended to show improvement at higher MAP levels, whereas those with normal baseline flow may see no improvement, or even a reduction, in flow. In some cases, CRT, a marker of microcirculatory flow, may either increase or decrease when vasopressors are used to raise MAP by the same amount in different patients (101). Additionally, if tissues have entered a state of senescence, simply restoring flow may not improve function. If perfusion pressure is normalized but organ function remains impaired, other factors beyond perfusion pressure are likely responsible for the dysfunction.

The ANDROMEDA-SHOCK trial introduced a test to assess macro-to-microcirculatory coupling by evaluating CRT responses to changes in MAP (102). A positive CRT response to higher MAP indicates that maintaining this higher MAP could be beneficial. Conversely, identifying patients where increasing norepinephrine doses worsen tissue perfusion signals the need to reconsider the MAP target.

Optimizing macrohemodynamics is only the first step in managing septic shock. While MAP is directly related to blood flow, normalizing it does not always improve microcirculatory conditions. MAP values greater than 65 mm Hg generally enhances TPP, which, in turn, may improve tissue perfusion, especially if Pcc is significantly higher than Pmsf. This improvement in MAP can be achieved through fluid resuscitation in fluid-responsive patients. However, if fluid alone does not raise MAP or improve Pcc, vasopressors should be initiated. If MAP exceeds 65 mm Hg and TPP is greater than 35 mm Hg, and the Pcc to Pmsf difference is greater than 10 mm Hg, but hypoperfusion persists, further fluid or vasopressor administration is unlikely to improve perfusion and may instead increase complications. But these final assumptions need to be formally tested before becoming standard practices.

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CONCLUSIONS

The relationship between arterial pressure and outcomes in septic shock is complex and heterogeneous. Focusing on critical parameters—such as TPP, the vascular waterfall, and individual treatment effects—enables a more personalized approach, focused on perfusion rather than pressure alone. Persistent hypoperfusion despite adequate macrocirculatory targets marks a pivotal moment when microcirculatory assessment becomes essential to guide therapy and avoid potentially harmful escalation of fluids or vasopressors. Bedside measurements of SAP, MAP, DAP, Pcc, and Pmsf offer practical tools for monitoring and tailoring treatment. Future clinical trials are needed to validate these metrics and refine resuscitation strategies in septic shock.

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